

71 peptide according to any of claims 38, 41, or 42, said antagonist or said agonist being capable of specifically binding to an opioid receptor-like 1 (ORL<sub>1</sub>) receptor present on a cell surface, said method comprising the steps of:

- preparing a cell extract from cells comprising a vector adapted for expression in said cells, said vector comprising a polynucleotide which expresses said receptor on the cells' surface;
- isolating a membrane fraction from said cell extract;
- incubating compounds present within said membrane fraction with said peptide under conditions permitting said peptide to bind specifically to said receptor;
- detecting the presence of compounds, if any, bound to said receptor; and
- recovering said bound compounds as the antagonist or the agonist.

52. (Twice Amended) A method for recovering an antagonist or an agonist of an isolated peptide according to any of claims 38, 41, or 42, said antagonist or said agonist being capable of specifically binding to an opioid receptor-like 1 (ORL<sub>1</sub>) receptor present on a surface of cells to prevent said isolated peptide from activating said receptor, said method comprising the steps of:

- contacting a cell comprising a vector adapted for expression in said cell, with a compound and said isolated peptide under conditions permitting measuring a functional response, said vector comprising a polynucleotide which expresses said receptor on the cell's surface;
- determining whether the compound prevents said isolated peptide from activating said receptor; and
- recovering the compound as the antagonist or the agonist if said compound does not activate said receptor.

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#### REMARKS

Upon entry of this amendment claims 35, 37-38, 40-42, 47, 51, 52, and 59 are pending. Claim 39 is canceled without prejudice to pursuing this claim in a continuing or related application. The claim amendments do not introduce new matter and a marked-up version of the claims showing where changes have been made is attached.

#### Rejection of claims 39-40, and 51-52 under 35 U.S.C. §102(e)

The Examiner has rejected claims 39-40, and 51-52 under 35 U.S.C. §102(e) as being anticipated by Grandy et al., U.S. Pat. No. 5,837,809. The Examiner states that Grandy et al. teach a ligand for a mammalian opioid receptor (SEQ ID NO: 5) which is 100% identical to the

sequence of SEQ ID NO: 2 recited in Applicants claim 39. Applicants submit that claim 39 is herein cancelled, and request that the rejection be withdrawn.

The Examiner states that Grandy et al. teach that the peptide can be produced by molecular or genetic engineering means, and that claim 40 is therefore anticipated. The Examiner further states that Grandy et al. teach a method of screening for agonists or antagonists of opioid binding to a receptor comprising expression of the receptor in host cells, isolation of cell membranes and use of the membranes to screen compounds for their effect on opioid binding activity, thus anticipating claims 51-52. Applicants respectfully traverse these rejections.

Claim 40 recites an isolated polynucleotide comprising a nucleic acid encoding a peptide selected from the group consisting of SEQ IS Nos. 2, 3, and 4. Applicants submit that Grandy et al. do not teach such a polynucleotide sequence. The Examiner cites col. 9, lines 27-28 of Grandy et al. as teaching polynucleotide sequence as claimed in Applicant's claim 40. Applicants submit that the cited passage teaches that "within the scope of this invention . . . are peptides made by molecular or genetic engineering means". Applicants submit that this mere suggestion of a means for generating the peptides taught in Grandy does not anticipate Applicants' claim to the specifically recited polynucleotide sequences of claim 40. Applicants submit that without an express teaching of the specific sequences recited in claim 40 (SEQ ID Nos. 2, 3, and 4) Grandy et al. does not anticipate this claim. As Grandy et al. do not teach the recited sequences, Applicants respectfully submit that this rejection is improper, and request that it be reconsidered and withdrawn.

Claims 51 and 52, as amended, each recite methods for recovering an antagonist or an agonist of an isolated peptide according to any of claims 38, 41, or 42. Claims 38, 41, and 41 recite an isolated peptide encoded by the nucleotide sequence of SEQ ID NO: 1, a peptide comprising the sequence of SEQ ID NO: 3, and a peptide comprising the sequence of SEQ ID NO: 4, respectively. Applicants submit that the Examiner has found each of claims 38, 41, and 42 to be allowable, that is, novel. Thus, Grandy et al. could not teach a method for recovering an

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antagonist or agonist of an isolated peptide of which Grandy was not aware. Applicants therefore submit that Grandy et al. do not anticipate either of claims 51 or 52, and request that the rejection be reconsidered and withdrawn.

### CONCLUSION

Applicants submits that all claims are allowable as written and respectfully request allowance of the Application by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney or agent would expedite prosecution of this application, the Examiner is cordially invited to call the attorney of record at 617-573-0451.

Respectfully submitted,

Date: \_\_\_\_\_

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### Marked-Up Version of Claims Showing Changes Being Made

51. A method for recovering an antagonist or an agonist of an isolated peptide according to any of claims 38, [39,] 41, or 42, said antagonist or said agonist being capable of specifically binding to an opioid receptor-like 1 (ORL<sub>1</sub>) receptor present on a cell surface, said method comprising the steps of:

- preparing a cell extract from cells comprising a vector adapted for expression in said cells, said vector comprising a polynucleotide which expresses said receptor on the cells' surface;

- isolating a membrane fraction from said cell extract;

- incubating compounds present within said membrane fraction with said peptide under conditions permitting said peptide to bind specifically to said receptor;

- detecting the presence of compounds, if any, bound to said receptor; and recovering said bound compounds as the antagonist or the agonist.

52. A method for recovering an antagonist or an agonist of an isolated peptide according to any of claims 38, [39,] 41, or 42, said antagonist or said agonist being capable of specifically binding to an opioid receptor-like 1 (ORL<sub>1</sub>) receptor present on a surface of cells to prevent said isolated peptide from activating said receptor, said method comprising the steps of:

- contacting a cell comprising a vector adapted for expression in said cell, with a compound and said isolated peptide under conditions permitting measuring a functional response, said vector comprising a polynucleotide which expresses said receptor on the cell's surface;

- determining whether the compound prevents said isolated peptide from activating said receptor; and

- recovering the compound as the antagonist or the agonist if said compound does not activate said receptor.